What is the safety and efficacy of platelet-rich plasma (PRP) in adults pertaining to wound healing and aesthetic rejuvenation? As use of PRP expands, a growing number of physicians and patients seek to answer this question. Barring large-scale clinical trials, a systematic literature review offers the best chance of answering this question. Per the Cochrane collaboration, a systematic review evaluates and compiles the findings of multiple clinical trials and provides best evidence to address the chosen research question. Conclusions can then be made and future recommendations suggested.

**SEARCH STRATEGY**

A comprehensive search of the current literature was undertaken using three databases—Cochrane Library, Medline via the Pubmed interface, and Google scholar—for an extensive review. The search parameters were limited to all English Language articles from 2006 to 2016, excluding animal studies, in vitro studies, and articles with no measurable endpoint.

The search strategy was designed to select all relevant articles via Mesh terms combined with key text terms to address our research question. Different constructs of search terms were formed by the implementation of truncation of the following terms: PRP wound healing, PRP facial rejuvenation, PRP, platelet-rich plasma, platelet preparations, PRFM platelet-rich fibrin matrix, growth factors, platelet therapy, platelet facial platelet wound healing, platelet plastic surgery AND facial rejuvenation or aesthetic rejuvenation or wound healing.

**SEARCH OUTCOME**

Initial search yielded 552 publications from Pubmed, nine from Cochrane Library, and 1,470 from Google Scholar. The search term was refined further to identify relevant articles, adhering to the steps of Prisma 2009. A review of the title and abstract of these papers was undertaken to determine their relevance to our research question, and this then yielded 23 potentially relevant papers. Scanning the references of these papers yielded further studies. Next, an in-depth analysis of these papers was carried out to ascertain the level of evidence, quality, and whether they met all of our inclusion and exclusion criteria. Six systematic reviews and one critical review were eventually extracted.
### TABLE 1. DATA ANALYSIS

<table>
<thead>
<tr>
<th>Author and date</th>
<th>Intervention</th>
<th>Sample size</th>
<th>Outcome Measure</th>
<th>Evidence level</th>
<th>Study reference</th>
<th>Weakness</th>
</tr>
</thead>
<tbody>
<tr>
<td>Martinez et al 2009</td>
<td>Tissue regeneration</td>
<td>20 RCTs</td>
<td>Oral and maxillofacial surgery, skin ulcers and surgical wounds.</td>
<td>1</td>
<td>1</td>
<td>20 quality RCTs found, based on Jadad scale which is outdated. Publication bias as no attempt to look at unpublished data. Results not reproducible. Methodological limitations due to heterogeneity and lack of description. Allocation concealment is questionable in the studies. Little data on safety. Small study size with large confidence intervals.</td>
</tr>
<tr>
<td>Villela et al 2010</td>
<td>Diabetic Ulcer</td>
<td>18 studies</td>
<td>Number of healed ulcers</td>
<td>1</td>
<td>2</td>
<td>Research question was too broad. Eligibility criteria was not defined. Heterogeneity and methodological flaws, example volume of blood used varied from 20 to 240ml. Poor reporting on the review process. Lack of data on the included studies, example intervention, control and treatment regimen.</td>
</tr>
<tr>
<td>Carter et al 2011</td>
<td>Wound healing in 3 main types of wounds, acute primary closure, acute secondary closure and chronic wounds.</td>
<td>24 papers (21 clinical studies and 3 systematic reviews)</td>
<td>PRP can positively impact wound healing, pain, and infection in both acute and chronic cutaneous cases. Complete wound healing, superficial infection and pain reduction. Wound area reduction, Wound depth, healing rate, time to heal, complications, Quality of life.</td>
<td>1</td>
<td>3</td>
<td>Wide variation in quality of studies and a risk of publication bias. Outcome measures for wound healing was too diverse.</td>
</tr>
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<tr>
<td>Taylor et al 2011</td>
<td>Tendon and ligament injuries</td>
<td>13</td>
<td>Constant score, MRI, serum cytokine concentration via Elisa assay,</td>
<td>1</td>
<td>4</td>
<td>From the studies, only 3 were RCTs. Wide variation in the method of collection, preparation, administration amongst the studies. Sample size was small in majority, with limited data and short term followup.</td>
</tr>
<tr>
<td>Wang et al 2014</td>
<td>PRP for treatment of acute wounds (meta-analysis)</td>
<td>13 articles involving 982 patients</td>
<td>Wound healing time, length of hospital stay, incidence of disturbed wound healing, post traumatic pain, wound infections. Findings: Use of PRP can shorten acute wound healing time and length of hospital stay, reduce the incidence of disturbed wound healing and blood products transfusion and alleviate post-traumatic pain, and wound infections.</td>
<td>1</td>
<td>7</td>
<td>Good statistical analysis with use of wide range of RCTs in the study. Role of publication bias. Wide variation in the method of collection, preparation, administration amongst the studies.</td>
</tr>
<tr>
<td>Leo et al 2015</td>
<td>Aesthetic Dermatology</td>
<td>22 manuscripts</td>
<td>Outcome measure not detailed. Benefit in scar revision, androgenic alopecia, post laser recovery and rejuvenation.</td>
<td>1</td>
<td>5</td>
<td>Bias Results not reproducible. Several studies lack controls, split-face comparisons. To better evaluate PRP efficacy and reduce inter-subject variability. Studies were often small scale, with few subjects. Lack of studies evaluating different forms of PRP and variation in the PRP collection process, which leads to difficulty in comparing studies.</td>
</tr>
<tr>
<td>Sclafani et al 2015</td>
<td>Facial rejuvenation and wound healing</td>
<td>61 reports, divided into in vitro, animal studies and clinical studies.</td>
<td>Varied outcome measures, positive effect on cellular changes, wound healing and facial rejuvenation.</td>
<td>5</td>
<td>6</td>
<td>Limitation: Reports varied widely in measurable endpoints.</td>
</tr>
</tbody>
</table>
CONCLUSION

Efficacy. Of the six systematic reviews and one critical review, five evaluated various types of wound healing from post-surgical ulcers, sports related, and two evaluated aesthetic rejuvenation. Studies varied in design, size, and power, hence this lack of uniformity results in complexity in comparison, and poor validity and reproducibility of findings. Reports varied in outcome measures.

In wound healing, common parameters used were complete wound healing, wound area reduction, wound depth, healing rate, time to heal, complications, example wound infection, quality of life, and pain reduction. As wounds cover a wide spectrum, from medical to post surgical, and consist of a wide degree of variation, the studies unfortunately did not indicate a detailed description of the type of wounds investigated to correct for inter wound variability.

In aesthetic rejuvenation, common parameters used were subjective doctor and patient evaluation, photo reviews, and objective skin biopsy, trichoscan hair measurements, etc. Noting the above variation in outcome measures, findings tend to lack statistical power. Several studies lacked controls and split-face comparisons. Studies were often small scale, with few subjects.

There is a high likelihood of publication bias favoring positive results with the use of PRP in both cases, which demonstrated positive effects on cellular changes, wound healing and aesthetic rejuvenation. Many of the studies demonstrated results that were difficult to quantify objectively. PRP treatment protocol lacked standardization for extraction, injection, dosing, and volume. Lack of studies evaluating different forms of PRP and variation in the PRP collection process, which leads to difficulty in comparing studies.

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**INCLUSION CRITERIA**
 Adults > 19 years old  
 Skin rejuvenation or Wound healing  
 Timeframe for 2006 to 2016  
 English language publications  
 Highest quality papers with level 1 evidence

**EXCLUSION CRITERIA**
 Animal studies  
 In vitro studies  
 Articles with no measurable endpoint

**ABBREVIATIONS:**
 RCT: randomized controlled trials  
 PRP: Platelet rich plasma

**Safety.** On the aspect of safety, PRP is superior to filler agents, with self-limiting minor side effects of swelling, erythema and bruising as per QMUL module 8 coursework. The above studies have not reported any long-term or permanent side effects.

**Clinical application.** With reference to the research question, our findings show that although results are encouraging, high level evidence and high quality RCTs are still lacking. That said, the evidence for wound healing appears to be more substantial than for aesthetic rejuvenation as seen by the quality, design, and number of RCTs.

There is still a wide variation in the types and uses of platelet preparation, with no universal standard. Combination of PRP with other modalities is a big scope for future evaluation, specifically the choice, dosing, sequencing, interval, and frequency.

Large robust RCTs are needed, however a suitable split-face intervention as a control to PRP has yet to be established. Another challenge would be the fact that pharmaceutical companies would hesitate to fund a trial with no intellectual property rights.

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Dr. Daniel Chang specializes in Aesthetic and Regenerative Medicine and is a Key Opinion Leader and Regional Trainer. Dr. Chang founded Asia Aesthetic Academy in 2015 and has developed a number of signature treatments, including the DC 3D-Dreamlift and the DC 3D-Noselfit. He maintains a Korean Aesthetics site and can be reached at drdanielchang.com

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